

Claims

1 A method for the diagnosis of a polymorphism in a PDH E1 α gene in a human, which method comprises determining the sequence of the nucleic acid of the human at position 1388
5 in the PDH E1 α gene as defined by the position in SEQ ID NO: 2, and/or at one or more of positions 26 and 161 of intron 7 of the PDH E1 α gene as defined in SEQ ID NO.1; and determining the status of the human by reference to polymorphism in the PDH E1 α gene.

2 A method according to claim 1 in which the polymorphisms are further defined as:

Position	Reference	Region	Polymorphism
26	SEQ ID NO:1	intron 7	(GGCCAA) _n
161	SEQ ID NO:1	intron 7	C/A
1388	SEQ ID NO:2	3' UTR	C/T

10 3 A method according to claim 2 which comprises diagnosis of the following haplotype:

Position	Reference	Region	Polymorphism
26	SEQ ID NO:1	intron 7	(GGCCAA) ₂
161	SEQ ID NO:1	intron 7	A

4 A nucleic acid comprising the nucleic acid of SEQ ID NO.1 or a sequence at least 85% homologous thereto; or a complementary strand thereof or an antisense sequence thereto or a fragment thereof of at least 20 bases comprising at least one positions 26 or 161.

15 5 An allele specific primer capable of detecting a PDH E1 α gene polymorphism at one or more of position 1388 in the PDH E1 α gene as defined by the position in SEQ ID NO: 2 and/or positions 26 and 161 of intron 7 of the PDH E1 α gene as defined by the positions in SEQ ID NO.1.

6 An allele-specific oligonucleotide probe capable of detecting a PDH E1 α gene
20 polymorphism at one or more of position 1388 in the PDH E1 α gene as defined by the position in SEQ ID NO: 2 and/or positions 26 and 161 of intron 7 of the PDH E1 α gene as defined by the positions in SEQ ID NO.1.

7 Use of any polymorphism as defined in claim 2 as a genetic marker in a linkage study.

position in SEQ ID NO: 2 and/or positions 26 and 161 of intron 7 of the PDH E1 α gene as defined by the positions in SEQ ID NO.1.

7 Use of any polymorphism as defined in claim 2 as a genetic marker in a linkage study.

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8 A method of treating a human in need of treatment with a PDH drug in which the method comprises:

i) diagnosis of a polymorphism in the PDH E1 α gene in the human, which diagnosis comprises determining the sequence of the nucleic acid at one or more of position 1388 in the

10 PDH E1 α gene as defined by the position in SEQ ID NO: 2 and/or positions 26 and 161 of intron 7 of the PDH E1 α gene as defined by the positions in SEQ ID NO.1, and determining the status of the human by reference to polymorphism in the PDH E1 α gene; and

ii) administering an effective amount of a PDH drug.

15 9 Use of any one of the following in bioinformatic analysis:

i) any polymorphism as defined in claim 1 or 2;

ii) the haplotype defined in claim 3; or

iii) a nucleic acid sequence as defined in claim 4.

20 10 A use according to claim 9 comprising a bioinformatic analysis selected from homology searching, mapping, haplotyping, genotyping or pharmacogenetic analysis.

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